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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,287	06/26/2001	Jennifer L. Hillman	PF-0334-2 DIV	2779

27904 7590 12/16/2002

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 12/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/892,287	Applicant(s) HILLMAN ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002 and 07 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11 and 30-45* is/are pending in the application.

4a) Of the above claim(s) *30,33,35,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,31,32,34 and 36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 July 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *9* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Changes

1. Applicant's amendments, filed 7/22/02 and 10/7/02 (Paper Nos. 7 and 10), are acknowledged. Claim 1 has been canceled. Claims 2-10, 12-29 and 46-47 have been canceled previously. Claims 11, 36-39, 41 and 44 have been amended.
Claims 11 and 30-45 *are pending.*

2. Applicant's election with traverse of Group II (claims 11, 31-32, 34 and 36-43) in Paper No. 7 (reiterated in Paper No. 10) is acknowledged.

The traversal is on the grounds that the method claim should be rejoined to claims of Group II as per In re Ochiai and In re Brouwer. This not found convincing at the present time because rejoinder of process claims to an allowable product claim is appropriate only once an allowable product claim has been identified. *Until an allowable product claim is identified,* claims to the non-elected invention are withdrawn from further consideration under 37 CFR 1.142.

In view of the rejections set forth below, the issue of rejoinder of claims 30, 33, 35 and 44-45 is held in abeyance.

Claims 30, 33, 35 and 44-45 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 11, 31-32, 34 and 36-43 *are under consideration in the instant application.*

Sequence Compliance

3. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

However, please see comments in the objection to the specification.

Drawings

4. The formal drawings submitted 7/22/02 have been approved by the Draftsman.

IDS

5. Applicant's IDS, filed 6/26/02 (Paper No. 11), is acknowledged.

Specification

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

It is suggested that Applicant amend the Title to read:
-- ANTIBODIES TO A PHOSPHATIDYLINOSITOL 4,5-BISPHOSPHATE 5-PHOSPHATASE --

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. The disclosure is objected to for the following reason:
Page 4 at line 18 discloses GI 1399105 as SEQ ID NO:3. However, SEQ ID NO:3, as set forth in the Sequence Listing, corresponds to GI 1399101.

Applicant is requested to verify the correct reference for the sequence shown in Figure 2A-2E. It appears that SEQ ID NO:3 is not the sequence shown in Figure 2A-2E as g1399105, and *the g1399105 sequence does not appear to have a corresponding sequence in the Sequence Listing.* If the g1399105 sequence shown in Figure 2A-2E is not represented in the Sequence Listing, Applicant is required to provide a new Sequence Listing, CRF, and Statement that the CRF and paper copy are the same which includes the g1399105 sequence.

Applicant is reminded to provide reasons as to why both the error and the correction of the error is obvious if any change is made to either the drawings, Brief Description of the Drawings, or Sequence Listing.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required:

> There does not appear to be clear antecedent basis for each of the individual method steps of claims 36 and 39; and therefore for the products of claims 37-38 and 40-41 produced by the methods of claims 36 and 39. Applicant is requested to identify support in the instant specification for each method step, particularly step "b" of claim 36 and steps "b", "c" and "e" of claim 39.

Claim Objections

10. Claim 34 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

The definition of an "antibody" provided on page 7 of the specification does not appear to encompass labeled antibodies. Thus an antibody that is labeled is broader in scope than the antibody in the composition of claim 32.

Claim Rejections - 35 USC § 112 first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 11, 31-32, 34 and 36-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for antibodies or fragments thereof which specifically bind SEQ ID NO:1 or immunogenic fragments thereof, does not reasonably provide enablement for antibodies or fragments thereof which specifically bind an isolated polypeptide comprising various naturally occurring "variants" of SEQ ID NO:1, as set forth in instant claim 11b. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented.

Applicant has disclosed antibodies to the polypeptide of SEQ ID NO:1, which is a phosphatidylinositol 4,5-bisphosphate 5-phosphatase.

The specification does not appear to disclose any other naturally-occurring polypeptides at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity. Neither does the specification appear to disclose which sequences of the polypeptide of SEQ ID NO:1 are essential for phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity.

The specification does not appear to be sufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. Despite knowledge in the art for producing antibodies to specific sequences, the specification fails to provide guidance regarding which polypeptide variant retains the instantly recited phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity. Furthermore, it is not routine in the art to screen large numbers of encoded amino acid variants where the expectation of retaining similar function is unpredictable based on the instant disclosure.

In addition, the specification fails to provide sufficient guidance as to the antibody epitopes in SEQ ID NO:1, either linear or conformational, that results in antibodies that bind the polypeptide of SEQ ID NO:1. Definition of the epitope(s) of a particular polypeptide recognized by an antibody is essential to both make and use an antibody to variants of the polypeptide of interest. Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444) teaches single amino acid substitutions **outside** the antigenic site on a protein effect antibody binding; thus it is also essential to provide some guidance as to the identity of the flanking sequences of a fragment of a polypeptide of interest. Further, Li et al. (Proc. Natl. Acad. Sci. USA 77: 3211-3214, 1980) disclose that dissociation of immunoreactive from other biological activities when constructing analogs (see entire document).

Thus in the absence of guidance to a particular epitope and the structural context in which the epitope is found; it is highly unpredictable which other isolated polypeptides comprising a variant sequence of SEQ ID NO:1 would maintain the relevant antibody epitope(s).

The scope of the claimed antibodies is not commensurate with the enablement provided by the disclosure with regard to the various isolated polypeptides comprising variant sequences as broadly encompassed by the claimed invention. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without further guidance as to the nature of the antibody epitope; it would require undue experimentation to make and use antibodies to variants of the polypeptide of SEQ ID NO:1. Consequently, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claim Rejections – 35 U.S.C. § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 11, 32, 34 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laxminarayan et al. (J. Biol. Chem. 1993; 268:4968-4974) in view of GenBank Accession #AAB03214 (Nussbaum, R.L., (GI 1399101, GenBank Sequence Database, Accession No. AAB03214, National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD 20894, Release Date 29 June 1996, Version AAB03214.1), as evidenced by the attached alignment.

The claims are drawn to polyclonal antibodies which specifically bind a polypeptide comprising the amino acid sequence of SEQ ID NO:1, or a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, or an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, as well as to methods of making said antibodies.

Laxminarayan et al. teach the purification and characterization of an inositol polyphosphate 5-phosphatase activity found in placenta (see entire document, e.g., Abstract). Laxminarayan et al. compared the placental 5-phosphatase to a previously identified 5-phosphatase from platelets using antibody-based assays such as immunoprecipitation and showed that the proteins having the 5-phosphatase activity in the two cell types were distinct proteins (see especially pages 4971-49772 "Immunoprecipitation of Inositol Polyphosphate 5-Phosphatase Activity").

Laxminarayan et al. thus teach that antibodies to proteins having 5-phosphatase activity can be used to characterize individual 5-phosphatases and clarify the molecular relationship among proteins of different molecular weight and found in different cell types, but having the same activity (see entire document).

Laxminarayan et al. teach compositions comprising the polyclonal antibody and a suitable carrier that is an acceptable excipient, since the polyclonal antibody in both serum and Tris-buffered glycine is taught (e.g., page 4969, right column, 1st partial paragraph).

Laxminarayan et al. further teach coupling the polyclonal antibody to protein A-sepharose (e.g., page 4969 "Immunoblotting and Immunoprecipitation"). Thus Laxminarayan et al. also teach a composition comprising the antibody wherein the antibody is labeled, since the polyclonal antibody bound to the protein A-sepharose are also a composition, and the protein A-sepharose acts as a "label" for the polyclonal antibody which allows detection of the antibody.

Laxminarayan et al. teach methods of producing polyclonal antibodies to 5-phosphatase proteins by immunizing animals with either whole 5-phosphatase protein, or immunogenic fragments of a 5-phosphatase protein (see page 4969 "Preparation of Antibodies" and "Preparation of Recombinant Fusion Proteins for Generation of Antibodies"). Laxminarayan et al. teach isolating antibodies from the immunized animals and screening with the polypeptide to identify polyclonal antibodies which specifically bind the 5-phosphatase (see page 4969, especially "Affinity Purification of Antibodies").

Laxminarayan et al. differ from the instant claims in that the 5-phosphatase is not a polypeptide comprising the amino acid sequence of SEQ ID NO:1, or a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, or an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

GenBank Accession #AAB03214 teaches a protein sequence that is a phosphatidylinositol (4,5)bisphosphate 5-phosphatase homolog.

The protein of GenBank Accession #AAB03214 from position 2 to position 329 is 99.4% identical to the polypeptide of SEQ ID NO:1 from position 45 to position 372, as evidenced by the attached alignment. Thus the protein taught by GenBank Accession #AAB03214 is a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, and an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

Although the protein of GenBank Accession #AAB03214 lacks amino acids 1-44 of SEQ ID NO:1, the ordinary artisan at the time the invention was made would have found it obvious to produce polyclonal antibodies to the protein of GenBank Accession #AAB03214 using the methods taught by Laxminarayan et al. The ordinary artisan would have been motivated to produce polyclonal antibodies to the amino acid sequence set forth in GenBank Accession #AAB03214 in order to isolate this protein, characterize this new 5-phosphatase, and compare it to other 5-phosphatase for which the molecular identity was not yet known. Alternatively, the ordinary artisan at the time the invention was made would have been motivated to produce antibodies to GenBank Accession #AAB03214 in order to characterize the cell type expression and subcellular localization of this 5-phosphatase.

As taught by Laxminarayan et al., at the time the invention was made, characterization of 5-phosphatases using polyclonal antibodies was well known in the art and the ordinary artisan had a reasonable expectation of successfully producing polyclonal antibodies to any 5-phosphatase of known sequence.

Finally, given the extensive homology between GenBank Accession #AAB03214 and the polypeptide of SEQ ID NO:1, any antibody produced to the 5-phosphatase of GenBank Accession #AAB03214 would necessarily specifically bind to each of a polypeptide comprising the amino acid sequence of SEQ ID NO:1, a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, and an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 11, 32, 34 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palmer et al. (J. Biol. Chem. 1994; 269(5):3403-3410) in view of GenBank Accession #AAB03214 (Nussbaum, R.L., (GI 1399101, GenBank Sequence Database, Accession No. AAB03214, National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD 20894, Release Date 29 June 1996, Version AAB03214.1), as evidenced by the attached alignment.

The claims are drawn to monoclonal antibodies which specifically bind a polypeptide comprising the amino acid sequence of SEQ ID NO:1, or a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, or an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1, as well as to methods of making said antibodies.

Palmer et al. teach the purification and characterization of two phosphatidylinositol 4,5-bisphosphate 5-phosphatases found in bovine brain cytosol (see entire document, e.g., Abstract). Palmer et al. teach the production of monoclonal antibodies to components of a partially purified preparation having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, and further teach that monoclonal antibodies to phosphatidylinositol 4,5-bisphosphate 5-phosphatases are useful tools to study the distribution, structure, and regulation of these two forms of phosphatidylinositol 4,5-bisphosphate 5-phosphatases (see entire document, as summarized in Abstract)

Palmer et al. teach compositions comprising the monoclonal antibodies and a suitable carrier that is an acceptable excipient, since the monoclonal antibodies in ascites fluid is taught (e.g., page 3404, "Preparation of Monoclonal Antibodies") and the monoclonal antibody in glycine is taught (e.g., page 3404 "Two-antibody Sandwich Assays").

Palmer et al. also teach labeling the monoclonal antibodies with biotin (e.g., page 3404 "Two-antibody Sandwich Assays" and Table III).

Palmer et al. teach the application of the monoclonal antibodies in a variety of assays for characterization of the phosphatidylinositol 4,5-bisphosphate 5-phosphatase, including immunoprecipitation, western blotting and ELISA (see entire document, especially page 3404, "Experimental Procedures" and Figures 5-7 and Table II and III).

Palmer et al. teach methods of making monoclonal antibodies by immunizing an animal with the partially purified enzyme, isolating spleen cells which includes the antibody-producing cells, fusing the spleen cells with an immortalized cell line to produce hybridomas, culturing the hybridomas and isolating from the hybridoma culture monoclonal antibodies (see page 3404, especially "Preparation of Monoclonal Antibodies").

Palmer et al. differ from the instant claims in that the phosphatidylinositol 4,5-bisphosphate 5-phosphatases is not a polypeptide comprising the amino acid sequence of SEQ ID NO:1, or a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, or an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

GenBank Accession #AAB03214 teaches a protein sequence that is a phosphatidylinositol (4,5)bisphosphate 5-phosphatase homolog.

The protein of GenBank Accession #AAB03214 from position 2 to position 329 is 99.4% identical to the polypeptide of SEQ ID NO:1 from position 45 to position 372, as evidenced by the attached alignment. Thus the protein taught by GenBank Accession #AAB03214 is a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, and an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.

Although the protein of GenBank Accession #AAB03214 lacks amino acids 1-44 of SEQ ID NO:1, the ordinary artisan at the time the invention was made would have found it obvious to produce monoclonal antibodies to the protein of GenBank Accession #AAB03214 using the methods taught by Palmer et al. The ordinary artisan would have been motivated to produce monoclonal antibodies to the amino acid sequence set forth in GenBank Accession #AAB03214 in order to isolate this protein, characterize this new phosphatidylinositol 4,5-bisphosphate 5-phosphatase, and compare it to other phosphatidylinositol 4,5-bisphosphate 5-phosphatase for which the molecular identity was not yet known. Alternatively, the ordinary artisan at the time the invention was made would have been motivated to produce antibodies to GenBank Accession #AAB03214 in order to characterize the cell type expression and subcellular localization of this phosphatidylinositol 4,5-bisphosphate 5-phosphatase.

As taught by Palmer et al., at the time the invention was made, characterization of phosphatidylinositol 4,5-bisphosphate 5-phosphatases using monoclonal antibodies was well known in the art and the ordinary artisan had a reasonable expectation of successfully producing monoclonal antibodies to any phosphatidylinositol 4,5-bisphosphate 5-phosphatase for which at least a partially purified preparation could be obtained.

Finally, given the extensive homology between GenBank Accession #AAB03214 and the polypeptide of SEQ ID NO:1, any antibody produced to the 5-phosphatase of GenBank Accession #AAB03214 would necessarily specifically bind to each of a polypeptide comprising the amino acid sequence of SEQ ID NO:1, a polypeptide comprising a naturally occurring sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 and having phosphatidylinositol 4,5-bisphosphate 5-phosphatase activity, and an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Claims 31 and 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over unpatentable over Palmer et al. (J. Biol. Chem. 1994; 269(5):3403-3410) in view of GenBank Accession #AAB03214 (Nussbaum, R.L., (GI 1399101, GenBank Sequence Database, Accession No. AAB03214, National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD 20894, Release Date 29 June 1996, Version AAB03214.1), as evidenced by the attached alignment; as applied to claims 11, 32, 34 and 39-41 above, and further in view of and further in view of Ramakrishnan et al. (US Pat. No. 5,817,310).

The claims are drawn to various forms of an antibody and methods of making antibodies by screening recombinant immunoglobulin and Fab expression libraries.

Palmer et al. in view of GenBank Accession #AAB03214 have been discussed supra and teach a monoclonal antibody to a polypeptide comprising an amino acid sequence of SEQ ID NO:1, methods of making and compositions comprising said antibody.

Palmer et al. in view of GenBank Accession #AAB03214 differ by not teaching chimeric, single chain, humanized or Fab/F(ab')$_2$ fragments of the antibody, nor by teaching that such antibodies can be isolated from Fab expression and recombinant immunoglobulin libraries.

However, one of ordinary skill in the art at the time the invention was made recognized that there were many ways to produce an antibody, and that the various forms of antibody were art-recognized variants of one another.

For example, Ramakrishnan et al. teach that the ordinary artisan at the time the invention was made recognized that antibodies could be formulated in any of a variety of interchangeable forms for use as compositions comprising a pharmaceutically acceptable carrier in a variety of art recognized assays to detect a protein of interest (see entire document, especially columns 8-17). Ramakrishnan et al. teach that antibodies can be single chain antibodies, Fab fragments, or F(ab')$_2$ fragments (see e.g. column 9 at lines 9-27), as well as chimeric or humanized antibodies (e.g., column 14). Ramakrishnan et al. also teach that it was well known in the art that antibodies to a protein of interest could produced by screening a recombinant immunoglobulin library which encode either the antibodies or fragments thereof (i.e. Fab) (e.g., see column 12 at line 56 to column 13). Further, compositions comprising antibodies in a pharmaceutically acceptable carrier, and various art recognized applications of antibodies for detection are taught in columns 15-17. Labeling of antibodies for use in various applications is also taught (e.g., column 11).

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to prepare antibodies in any of the instantly recited forms for use in art-recognized assays such as those of western blotting, ELISA and immunoprecipitation as taught by Palmer et al. The ordinary artisan would have been motivated to make these various forms of antibodies in view of the art-recognized interchangeability of the different antibody forms and in order to provide a variety of detection reagents that could be used in detection assays such as the western blotting assay taught by western blotting, ELISA and immunoprecipitation as taught by Palmer et al. The ordinary artisan recognized the advantage of antibody variants for use in such detection assays because depending upon the other antibodies used in combination, the antibody variants could be labeled using differential secondary reagents, thus avoiding high backgrounds in ELISA and immunoblotting assays. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
December 11, 2002

Phillip Gambel
PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
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12/16/02